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*R. J. Gerrits*

# ASSESSMENT OF NUCLEAR MAGNETIC RESONANCE RESEARCH WITHIN THE AGRICULTURAL RESEARCH SERVICE

Prepared for

The USDA/Agricultural Research Service

by

The ARS Nuclear Magnetic Resonance

Assessment Team

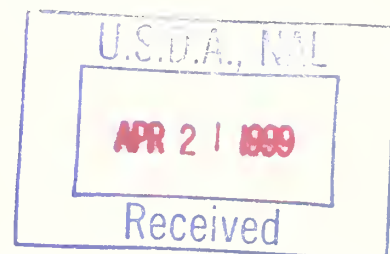
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A Status Report on Nuclear Magnetic Resonance  
Research Capabilities in the United States Department of Agriculture  
Agricultural Research Service



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## Table of Contents

Executive Summary .....	4
Recommendations .....	5-7
Introduction .....	8
Documentation	
A. Magnetic Resonance Methods and Agricultural Applications: An Overview .....	9-11
B. Advantages and Disadvantages of Using NMR Instruments Outside of ARS .....	12-14
C. Nuclear Magnetic Resonance Spectrometers: Availability Within ARS and Cost of New Instrumentation .....	15-19
D. Efficient and Effective Use of NMR Instruments .....	20-21
E. Applications of NMR Imaging Spectroscopy in Agricultural Research	
1. Animal Studies .....	22
2. Insect Studies .....	23
3. Plant Studies .....	24-25
F. Criteria for Giving NMR Collaborators Recognition	
1. Part I .....	26-28
2. Part II .....	29-30
G. Selection of NMR Spectrometry and Imaging on a Merit of Proposal Basis .....	31-33
Acknowledgments .....	34
List of Participants .....	35
Appendix	
A. ARS Instrument Distribution List .....	36
B. ARS Instrument Distribution Map .....	37
C. Specific ARS Instrument and Personnel Needs .....	38



## Executive Summary

Nuclear magnetic resonance (NMR) instruments are unrivaled tools for analytical chemistry, in vivo metabolism studies and in vivo imaging. The capability of combining studies of NMR characterized chemical and physical properties of substances with in vivo techniques has opened a new frontier. All biological research disciplines have paths that lead to significant questions to which only NMR can give a definitive answer. ARS research demands stretch across many fields, nutrition and metabolism, toxicology and genetics, to name a few. All require data for structural identification and dynamics, and physical/chemical mechanisms that only NMR research can provide.

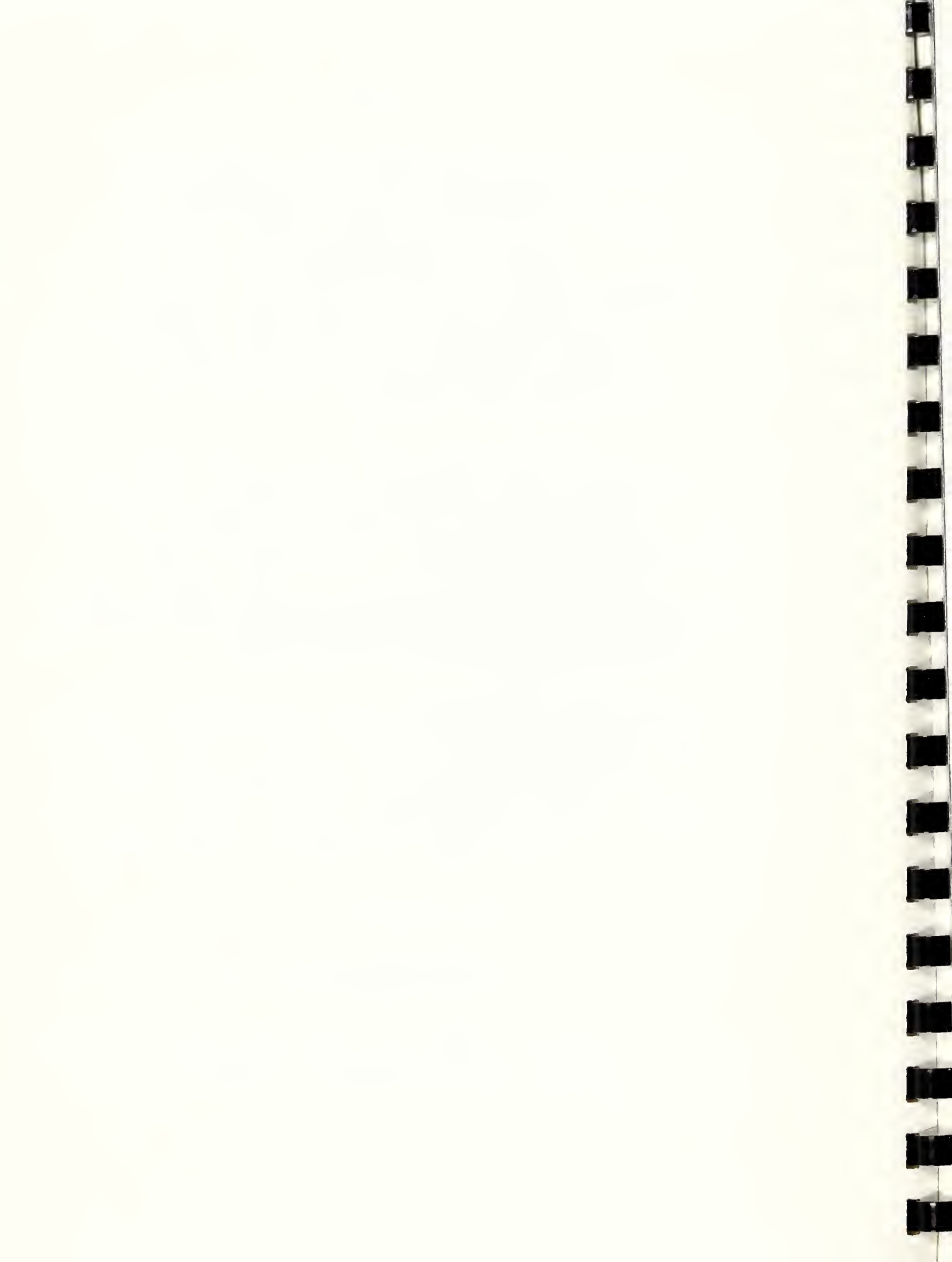
Several concerned scientists working through Dr. T. J. Army convened in Beltsville on March 3, 1986, to assess seven topics listed on the agenda (see page 3, Documentation A-G). The assessment team weighed all the information generated from the agenda. They deliberated at length and concluded that given the extent and distribution of NMR technology within ARS, the present instrumentation is inadequate in either number or kind to meet the present and future agricultural research demands.

The rate at which ARS is currently upgrading NMR instrumentation (only one 200-300 MHz request being considered at present) does not match the rapid rate at which NMR instrumentation is becoming obsolete. This situation is occurring during a time in which 68% of our current NMR instrumentation is already obsolete. ARS will soon be unable to provide the state of the art NMR support that is crucially needed by the agriculture research effort.

The following is the most critical implication:

*Within five years NMR support for ARS research programs  
will be insignificant.*

The team made recommendations (pages 5, 6, 7) for administrative actions that could restore NMR research in ARS and strengthen its posture as a first rate research organization.



## Recommendations

NMR research has an essential place in agriculture. The recommendations below provide strategies that could reduce the present NMR deficiencies in equipment and personnel in ARS and establish a framework to ensure that ARS has a future in NMR supported research.

### I. Action Required to Offset Obsolescence

Presently, 17 out of 25 NMR instruments in ARS are obsolete (see Appendix C for list of needs). The work required, without any guarantee of publishable results that could take three years, can now be accomplished with a good chance of usable data within three months or less provided that state-of-the-art instruments are made available. Actions for correcting this condition follow:

- A. Make a commitment to a five year replacement time frame. It appears unlikely that such large equipment purchases can be funded from individual or small clusters of Cris Work Units. Therefore, we recommend that where necessary these instruments be purchased from a larger budget base.

- 1. First Year

- Purchase three 200-400 MHz instruments - \$1,200,000

- 2. Subsequent Years

- Second year - Purchase one high field 500 MHz instrument - \$600,000.
    - Third year through fifth year - Purchase and/or upgrade two instruments/year - \$800,000/year.

### II. Establishment of ARS High Field Facility

- A. High field NMR in the 500 to 600 MHz range. This facility could be located in a geographically central location and managed by a highly competent ARS spectroscopist. The cost would be between \$500,000 to \$600,000. By replacing a 300 MHz instrument at an existing NMR facility with a high field instrument, the 300 MHz unit could be transferred to a research unit that is seeking funds to replace their inadequate instrumentation.

### III. Establish NMR Imaging Facility

- A. Presently, ARS does not have any NMR imaging capability. All imaging work has been carried out through informal agreements with state institutions and industrial firms. Two actions could improve the present status of ARS NMR imaging work.

- 1. Combined solid-state and small imaging capabilities. Fulfillment of instrumentation requirements for two 200 MHz solids instruments with imaging options (see Appendix C, page 38).



2. Combined Federal and State imaging resources for large capacity capability. Presently, a state facility exists in which ARS could install an instrument and house a spectroscopist who would serve as a national support person for many ARS/NMR imaging needs. The scientist in charge of this state facility is an inventor and world-acclaimed leader in the area of NMR imaging research. Similar arrangements may be possible with other state or private groups. The placement of an ARS spectroscopist with an ARS/NMR instrument is considered to be a primary consideration for the success of a state/federal or private/federal sharing relationship.

#### IV. Establish a Tritium NMR Capability

A. Although modern spectrometers have inherent tritium capabilities, an ARS location for this facility should include expertise in handling radio isotopes, a radiation protection officer, and licensing for disposal. Presently, no ARS location is carrying out tritium NMR studies.

#### V. NMR Use Efficiency

A. Improve NMR use efficiency through peripheral online data access, instrument control, and automation.

1. Develop an open shop operation that will give NMR users off location access to an NMR instrument through telephone line time sharing programs.

2. Support stacking and data acquisition programs with automatic sample changers on instruments that have a heavy load of routine experiments. Sample changers cost about \$30,000 and have an instrument life of about 10 years.

#### VI. Proposed ARS Policy for Use of NMR Facilities

A. Develop a procedure and document to formalize access to NMR facilities. Interim arrangements could possibly be worked out within the ARS by negotiating for time on the instruments listed in Appendix A.

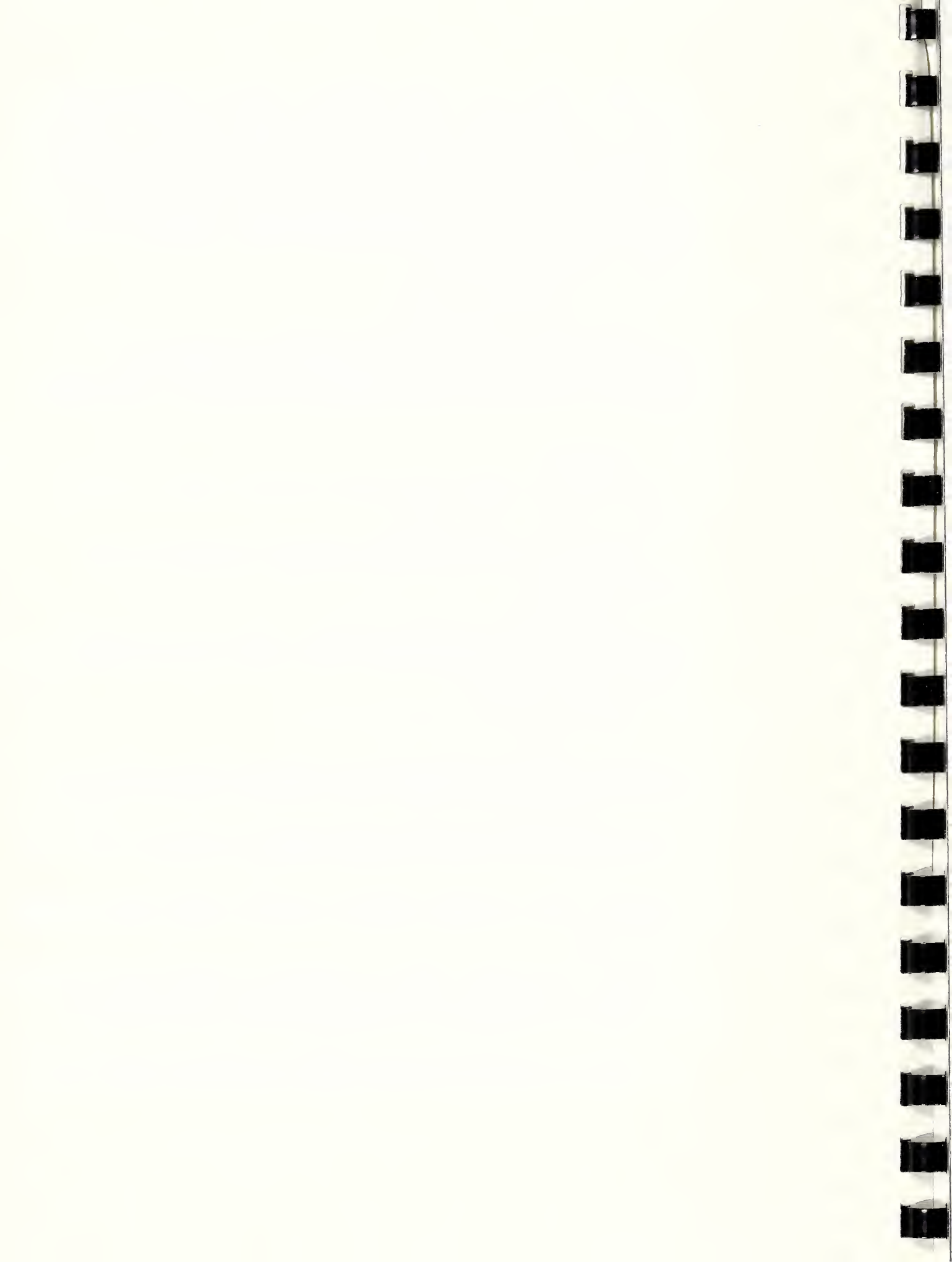
B. A peer review system should be established to rank ARS national NMR projects according to merit of proposal (see pages 31-33).

C. Establish a fiscal reserve that can be used to support peer reviewed and administratively approved projects in the event that location funds are inadequate.

D. Scientists who require "hands on" operation for their NMR experiments at NMR facilities away from their home locations could function more effectively and efficiently by the implementation of the following:

1. Support of travel needs for scientists carrying out projects that peer review determines acceptable based on merit (see pages 31-33).





2. Establish a visiting scientist sleeping quarters on or near the ARS NMR location with a telecommunications link to the NMR instrument (see page 21).

- E. Establish an electronic bulletin board to facilitate communication between NMR resource personnel. It would be used to share information, answer questions, recruit assistance or a source of instrumentation for difficult problems, and develop a report on interim solutions for dealing with NMR instrumentation shortage and obsolescence.

#### VII. Implement a Policy for Giving NMR Collaborators Recognition

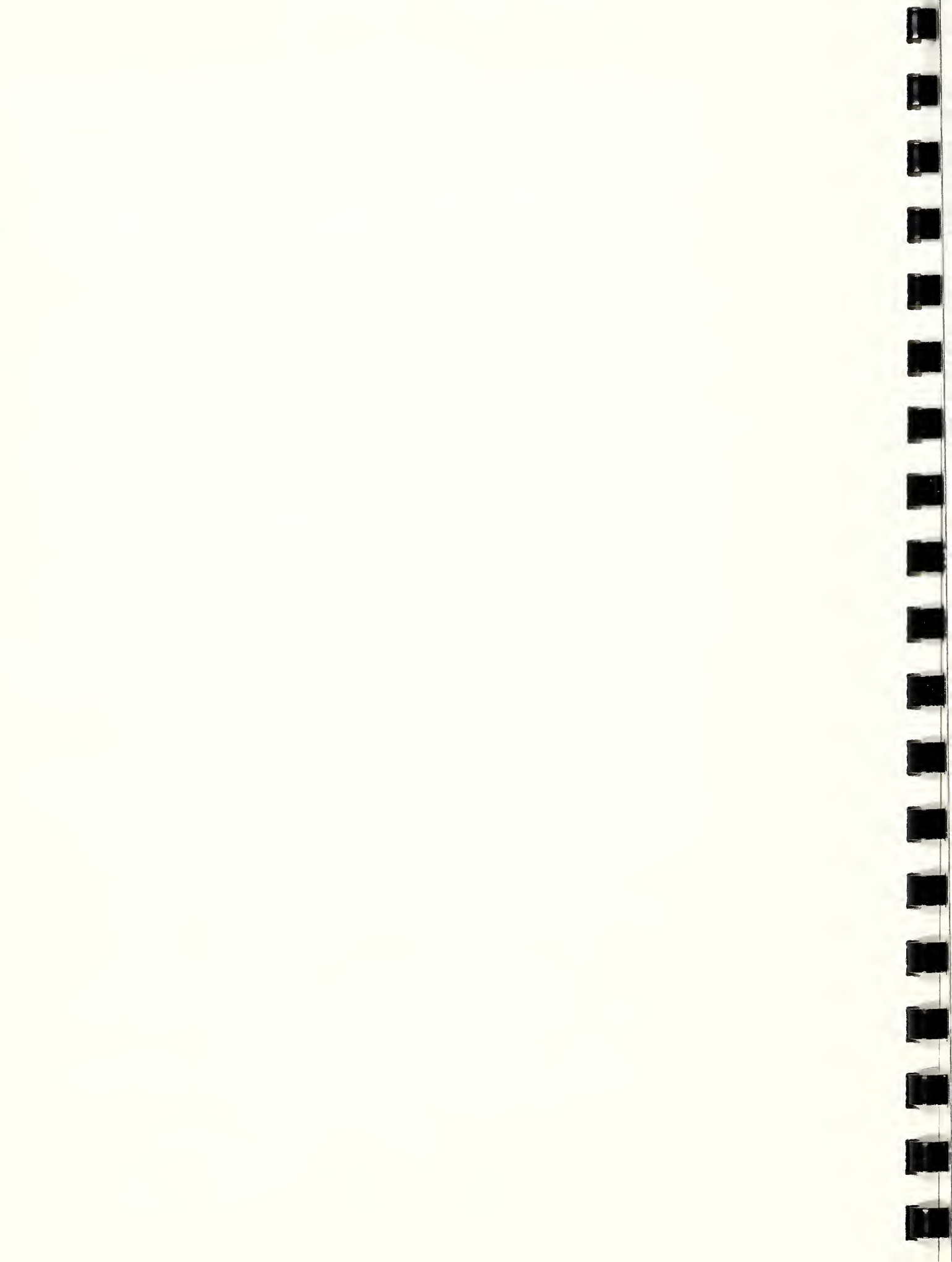
Criteria for a collaborator recognition policy are presented on pages 26-30.

#### VIII. Establish a National ARS, NMR Network

A. Scientists with interest in NMR research would contribute to a national project, overseen by a coordinator, who would work in concert with an NPS scientist to achieve the goals and objectives of the NMR network. Each year a workshop would be conducted to assess progress, reassess needs and revise plans and objectives as needed with an NPS scientist as the overseer.

B. The goal of the NMR network would be: To enhance the use of NMR spectroscopy to solve agricultural problems. The following objectives would support that goal:

1. Establish an ARS database for NMR spectra to permit sharing of data and to provide for the comparison and correlation of NMR data among different instruments.
2. Reevaluate the state of ARS/NMR capability each year.
3. Function as the peer review panel in defining priority, approach, and instrumental requirements for ARS problems requiring NMR technology.



## Introduction

A resurgence in NMR technology has evolved through recent advances in superconducting magnets and computer program innovations. These advances make NMR the most powerful tool available for analytical agricultural research. High field NMR is used to solve some of the most perplexing solution-state chemical structure problems. Solid state NMR gives access to determining the nature of samples not readily soluble in conventional NMR solvents. NMR imaging provides a non-invasive and non-destructive analysis of insects, plants, and animals for evaluating physiological events in a morphological context. Wide-line, low resolution NMR studies allow for assessment of gross sample composition.

The assessment team worked together with the intent that their efforts would provide guidance to enhance the decision making processes that keep the ARS strong contenders in the advancement of science. The team focused on finding ways to insure that NMR technology is available to support ARS research and that routine NMR analyses are available to remote ARS locations and are provided by the closest NMR instrument capable of performing the study.

The team received its mandate to assess ARS, NMR capabilities and potential through Dr. E. T. Littledike, USDA, ARS, National Program Staff, in his memo of November 4, 1985. Dr. Littledike proposed a set of guidelines for establishing the current status and future needs of NMR research in ARS. Team members were selected after a nationwide survey of ARS laboratories to determine the distribution of NMR instruments within the agency. An agenda was developed for addressing the seven topics listed by titles in the index and presented as follows.



# Magnetic Resonance Methods and Agricultural Applications: An Overview

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## I. High Field/High Resolution NMR Spectroscopy

### A. one and two dimensional methods: COSY, NOESY, INEPT, INADEQUATE

- i. structural identification: mycotoxins; pesticides and pesticide metabolites; new compounds derived from plants; new materials derived from agricultural by-products (animal fats, whey-derived lactose,  $\beta$ -lactoglobulin,  $\alpha$ -lactoglobulin); structure, conformation and branching of polysaccharides, both microbial- and plant-derived (pectins, mannans, starches, etc.).
- ii. structural dynamics: lipid/protein interactions at interfaces and in stable food emulsions and model membranes; measurement of bound water and suppression of water activity associated with food proteins; photosynthetic membrane processes; plant lectin binding. Principally use of  $^1\text{H}$ ,  $^2\text{H}$  and  $^{13}\text{C}$  NMR enrichment techniques.
- iii. mechanisms: elucidation of biosynthetic pathways using  $^2\text{H}$  and  $^{13}\text{C}$  enrichment, in vitro studies of metabolic pathways.

## II. In Vivo NMR

### A. Microorganisms:

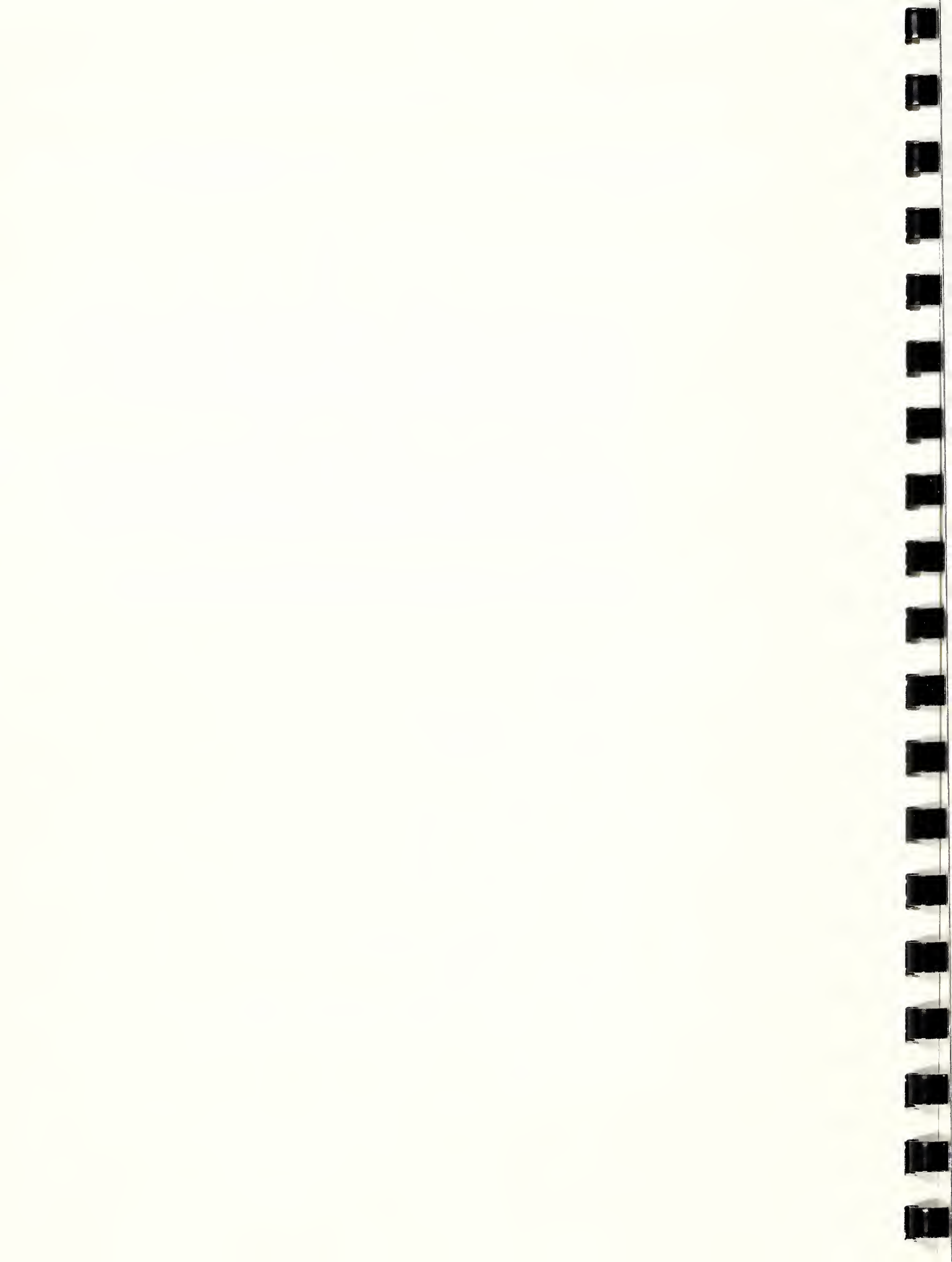
- i. generation of metabolites
- ii. fermentation processes
- iii. toxin production

### B. Animal Tissue ( $^{31}\text{P}$ and $^{13}\text{C}$ ):

- i. enzyme deficiency disease
- ii. metabolic disorders
- iii. chemistry of abnormal tissues
- iv. development of embryos

### C. Plant Tissue ( $^{31}\text{P}$ , $^{13}\text{C}$ , $^{23}\text{Na}$ , $^{39}\text{K}$ , $^{14}\text{N}$ & $^{15}\text{N}$ ):

- i. nutrient uptake





- ii. metal ion transport (toxic and non-toxic)
- iii. evaluation of hypoxia, also effects on ion transport
- iv. bioenergetics and metabolism:  $^{13}\text{C}$ ,  $^{31}\text{P}$  &  $^{13}\text{C}$ - $^{15}\text{N}$  double cross polarization
- v. evaluation of genetic defects (enzyme deficiency) in plants
- vi. seed analysis:  $^{13}\text{C}$  lipids, proteins, carbohydrates, breeding programs

### III. Solid State Nuclear and Paramagnetic Resonance

#### A. $^{13}\text{C}$ Cross-polarization/magic angle sample spinning NMR

- i. useful for routine composition determination of substances with limited solubility
- ii. relaxation properties
  - a. homogeneous -- vs -- heterogeneous mixtures
  - b. determination of differing domains of molecular or side chain motion
- iii. examples:
  - a. specific examples: demonstrated that secondary cell wall cellulosic compounds are closely associated with lignin; used to estimate the size of the aquoshell of divalent cations bound to anionic cell wall polymers; paramagnetic ion-induced  $^1\text{H}$  and  $^{13}\text{C}$  relaxation was used to demonstrate that the cationic species was finding in spatially discrete (non-random) regions
  - b. other: studies of soils (metal & organic compound binding site properties) --  $^{23}\text{Na}^+$  &  $^{13}\text{C}$  clays -- Si &  $^{31}\text{P}$  studies of phosphate sorption; protein structure -- collagen, silk (helix analysis); forage analysis; seed studies
- iv. present needs require the newest generation of spectrometers: higher fields, greater sensitivity, more nuclei, greater spectrometer control

### IV. Imaging

- A. NMR imaging: recent development; not used widely; mainly medical applications
  - i. unique advantages over microscopic and other imaging techniques



- a. can spatially resolve the relaxation behavior of  $H_2O$
  - b. noninvasive -- fewer artifacts
  - c. combination of images with specific volume spectra -- can ascertain the relative concentration of various nuclei
  - ii. major limitation: image resolution is on the order of only 100  $\mu m$  -- only observing at the supercellular or tissue level
- B. EPR IMAGING: very little has been developed
- i. advantage over NMR imaging: excellent spatial resolution -- ~ 400-500  $\text{\AA}$
  - ii. disadvantages:
    - a. g-values (equivalent to chemical shift in NMR) of the most interesting probes are quite similar -- overlapping signals
    - b. in biological samples have problems of microwave absorption; due to the high  $H_2O$  activity



# Advantages and Disadvantages of Using NMR Instruments Outside of ARS

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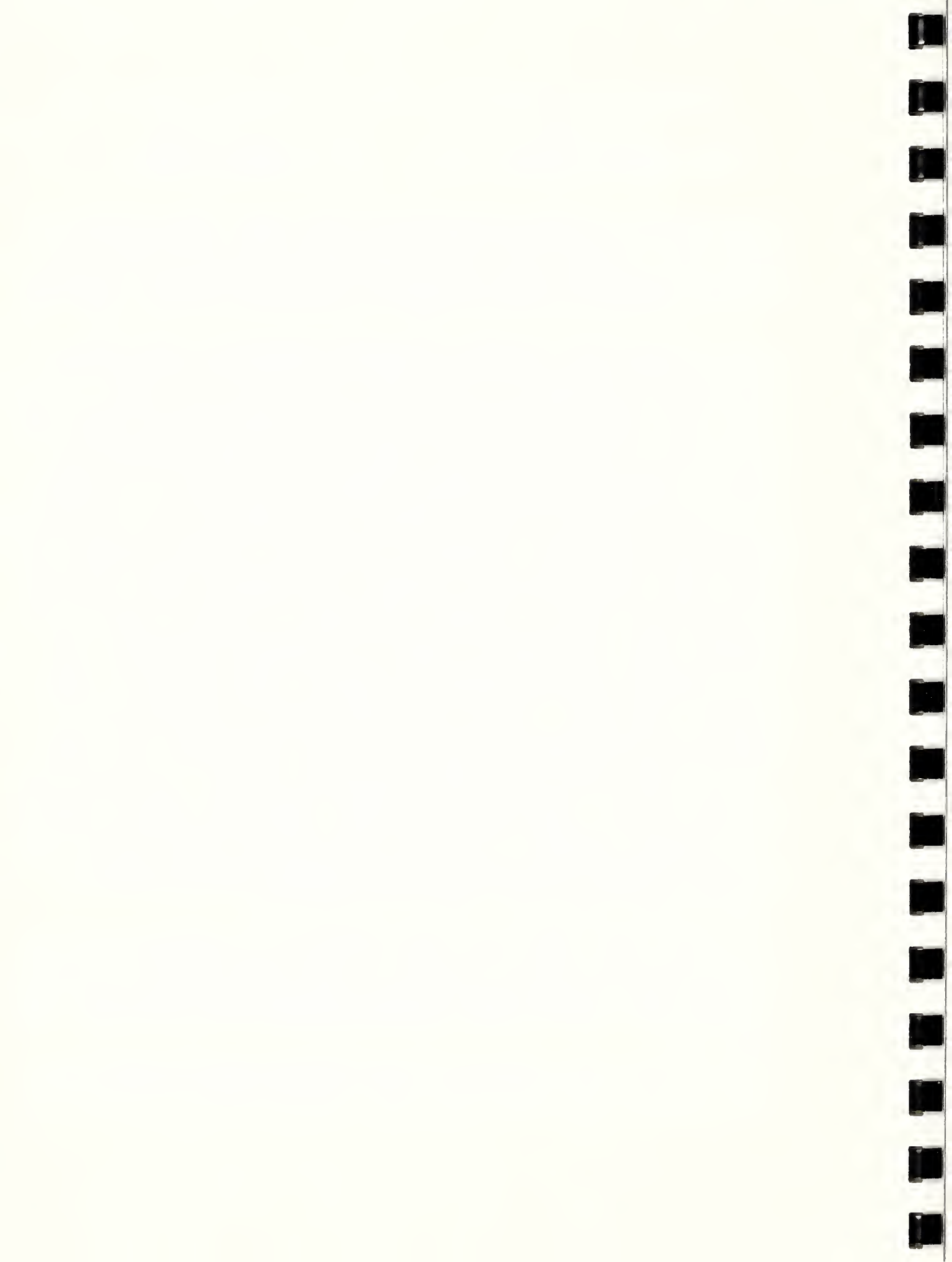
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Dawson, Georgia

We have decided to divide our presentation in two parts. First, an historical synopsis of our experiences with NMR co-operators, within and without the agency, which will have several common denominators for those of you involved with these exercises. Second, an objective, and therefore factual, accounting list of the advantages and disadvantages of using NMR instruments outside ARS.

In the late 1960's and early 1970's the science of NMR was in its infancy. It was, for the most part, a device for obtaining confirmatory information that complemented mass spectral, UV, and IR data. Additionally, the exact number of protons could be determined and functional groups could be ascertained. At that time we were isolating biologically active natural products and found NMR to be quite useful though we did not anticipate the quantum advances that were to be made in the next decade and a half. Because we were in field stations and because of limited budgets we quickly realized (in 1968-69) that we needed to find an individual who could make NMR analyses with proficiency. We thought that we had struck pay dirt when we located an NMR specialist with an up-to-date instrument in Beltsville. The machinery was set in motion and we approached our Branch Chiefs, letters were written, and a great deal of time and dialogue were expended to officially set up the program. We sent samples to the co-operator and sat back to await the results. Remember, the metabolites that we had sent had been hard to come by. We waited, and waited, and waited. We made repeated telephone calls. And we believe that those samples are still tucked away in some dark corner in Beltsville. Luckily, our co-operator was called to his eternal reward, thereby saving everyone a good deal of embarrassment. Also, it gave us a chance to look for another co-operator. About that time our luck changed for the better. In 1971, the confluence of two events led to a very effective collaboration. One of us had given a seminar at the University of Georgia that was attended by Richard K. Hill who, in turn, wrote us a letter telling us about a brilliant young spectroscopist - Richard Cox. The other had arrived at Dick Cox's name by making independent inquiries. And Cox was very anxious to help us. The situation synergized. The Georgia Commodity Commission for Tobacco gave us \$5,000 to buy a microprobe and this was matched by \$5,000 from the State of Georgia. At the same time,  $C^{13}$  NMR was coming into its own. We kept Cox pinned down with metabolites for analysis and that, coupled with his teaching assignments, plus work for other colleagues in the University of Georgia Chemistry Department, filled his working hours.

In 1972, our Agency bought us a 60 MHz, Jeol, NMR. We had split the bill, had the blessings of our Branch Chiefs, and the instrument was located in Tifton, Georgia. That instrument was a champion. We were running NMR's for scientists in Beltsville! But other important changes were beginning to take place in the science of NMR. There were more powerful instruments,  $C^{13}$  was becoming a very useful tool.

Towards the end of 1976, Richard Cox moved to NIEHS, Research Triangle Park, North Carolina. Now we were in high gear: the publications were rolling out



and Cox's reputation as an NMR spectroscopist were escalating. And we had access to even better equipment costing perhaps \$400,000 at no expense to ARS. But like all bubbles, it had to burst. Cox had become so proficient that industry became attracted to him and they made him an unrefusable offer. We thought that it was great. We had helped him to build his career and this was the payoff. We felt responsible for his success. Besides, we now had access to even more sophisticated equipment. What was it, \$1,000,000 - \$1,500,000? And at a cost of nothing to ARS. There were no parts to buy, no technician's salary, no overheads, and input from one of the world's best NMR jockeys.

However, industry decided that Cox had management potential (rightly so, they were, after all, paying his salary). Novel metabolites took longer and longer to resolve. Some remained a year-and-a-half. Others deteriorated. Data were collected but time could not be taken to analyze and construct the molecules. Some metabolites, which were very difficult to obtain, were re-isolated two or three times, still with no results. But metabolites that one suspected of being a certain structure were run quite quickly and the nature of the compound confirmed.

We cast our net around for other co-operators. The University of Chicago handled two compounds in six years and this led to one publication. This was painfully slow. Merck put important compounds on the 'back burner' because they were backed up with samples and, importantly, while they could run the samples with ease in the instrument, they could not spare the expertise to analyze the data.

Another agreement was made with BASF. We would supply them with new metabolites for screening and analysis. A compound was sent in November, 1985, and we still are awaiting results. Obviously this is a sweet deal for BASF because they will be first to see the structures and it is obvious that they will search their files for analogs.

We have approached colleagues in ARS to work on our problems and this has elicited two responses. They feel that they already have plenty of work (it is easy to reach overload within a short time), or they feel that this is service work. Because of the accounting system (senior author receives 3 points, second author 2 points, third 1 point and fourth 0) spectroscopists do not want to become involved. Our publication record indicates that NMR spectroscopists can, and have been senior authors. Nevertheless, our comments and proof do not settle colleague's fears.

Placement of a high quality instrument at a location does not suppose that the expertise is also available. We have no difficulty obtaining spectra from any of several sources. We do have difficulty in obtaining the necessary expertise to evaluate the data. And the field of NMR research has become highly sophisticated. Frankly, we no longer have the ability to interpret NMR data for our colleagues as we did 15-20 years ago.

We do have a potentially profitable situation at the Richard B. Russell Research Center. Peter Albersheim has a 250 MHz and a 500 MHz NMR that will be installed. For a reasonable fee (250 MHz, \$25/hr if we use our man; \$35/hr if we use their man. 500 MHz, \$50/hr and \$75/hr, respectively) we will have access





to these instruments. But, to reiterate, our problem is not access to instrumentation, it is access to adequate interpretive expertise.

The disadvantages of using the NMR instruments outside ARS may be enumerated as follows:

- (a) Expertise is available, but at 'their' convenience.
- (b) No priority for samples.
- (c) May be charged for samples.
- (d) Difficult to obtain patent. Collaborators know structure before chief investigator.
- (e) Easy to overload NMR spectroscopist with samples.
- (f) Authorship may be in dispute.
- (g) Material may be taken by spectroscopist and published giving ARS only an acknowledgment.
- (h) Labile materials may decompose before delivery, or examination.

The advantages of using NMR instruments outside ARS are:

- (a) No investment in equipment (no capital expenditures).
- (b) No maintenance of equipment (repairs, etc.).
- (c) No investment in personnel.
- (d) No overhead expenses.
- (e) Access to state-of-the-art equipment.
- (f) Access to highly qualified, experienced personnel.
- (g) Authorship position on papers not such an issue.
- (h) Stretches the scientific limit of companies (i.e., adds new programs to their software).

Other considerations also need to be evaluated. For example, the relationship between scientists can spell success or failure for a project. Two scientists whose personalities complement each other can execute volumes of work together, even if they are not brilliant. Two brilliant scientists who detest each other will accomplish exactly nothing and may destroy projects that involve other people. Furthermore, because of the complexity of skills required to analyze NMR data in various areas (solid state, natural products, etc.) and the fact that we may not be able to have all the expertise and all the instrumentation, perhaps a mixture of non-ARS and ARS instrumentation and expertise is the best approach to our problems at present. But, if ARS has an expert at a location, support that expert with sufficient equipment and funds.



Nuclear Magnetic Resonance Spectrometers: Availability Within ARS  
and Cost of New Instrumentation

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Vern Feil  
USDA/ARS/Metabolism & Radiation Res. Lab  
Fargo, North Dakota

Presently Operating Spectrometers

A survey (Appendix A) conducted by Dr. Gassner indicated that ARS presently has 25 nuclear magnetic resonance (NMR) spectrometers. Over two-thirds of these are electromagnetics of 2.35T (100 MHz) or less. Eight spectrometers have superconducting magnets of 4.7T (200 MHz) or higher field. The distribution of these spectrometers is shown in Appendix B.

New Equipment

A list of commercially available spectrometers of 200 MHz or larger (e.g., superconducting) is given in Table 1. This list does not include all models from every vendor. The price generally includes a very limited number of standard accessories. A summary of these prices is given in Table 2.

Comparison of Spectrometers: Conventional Electromagnetic vs. High Field Superconducting Magnetic

**Power Requirements:** Superconducting (SC) magnetic systems use less total electrical power than conventional electromagnets. However, SC magnets require liquid He and liquid N<sub>2</sub> to keep the coils at superconducting temperatures. In College Station, Texas, the estimated annual cost for these coolants for a 300-400 MHz magnet is \$750. For a 100 MHz conventional electromagnet the annual electrical cost, at \$0.55/kilowatt hour, is estimated to be \$4,300. The annual electrical cost for an SC magnetic is estimated to be \$1,200.

**Power Fluctuations:** Small fluctuations in power have a more pronounced effect on experiments conducted with a conventional electromagnetic system than with an SC system. An untimely power flicker can result in a 24 hour delay in an experiment while the electromagnet reequilibrates.

**Coolants:** As indicated above, SC magnets require a supply of liquid He and liquid N<sub>2</sub>. Isolated locations that do not have nearby industrial uses of He (e.g., heliarc welding) or become isolated for extended periods because of adverse weather conditions could encounter delivery problems that could result in a magnet quench, a potentially costly failure.

**Computer Capability:** Newer instruments have faster computers with 20, 24, or 32 bit processors. These provide the instrument with a large dynamic range, an important feature when working with dilute samples. Additional microprocessors designed to accomplish a specific function are common.

**Sensitivity:** As field strength increases, sensitivity also increases. Newer SC systems have improved electronics, giving a better signal to noise ratio.



Increased sensitivity decreases sample run time, allowing more efficient use of the instrument.

**Peak Separation:** As field strength increases, the distance between individual resonances (e.g., peaks) also increases. In  $^1\text{H}$ -NMR this is especially important in the interpretation of the spectrum. As the chemical shift differences between coupled protons increases, the coupling pattern changes from a higher order, which is difficult or impossible to analyze, to a first order coupling which is readily analyzed.

**2-D NMR Experiments:** New instruments are designed to perform 2-D experiments which are powerful aids in the structural analysis of compounds. These experiments require multiple sets of spectral accumulations using slight differences in the times of the pulse sequence. Greater sensitivity decreases the amount of time required to obtain the necessary signal to noise ratio during any set of accumulations. Since multiple sets are required, the time saved per set can routinely be multiplied by 500 to 1000. After all sets of accumulations are complete, complex computations are required before the results can be observed. Older electromagnetic spectrometers were built prior to the conception of these experiments. Their reduced sensitivity, slower computing capability, and software and hardware which were not designed to display and manipulate the results, combine to make these experiments beyond the reach of most older instruments.

**Other Nuclei:** The continuous-wave instruments (i.e., T-20, EM-360, EM-390) are generally useful only for proton NMR. Carbon NMR, essential in many research projects, should be available via all of the FT instruments in ARS; however, some of the older FT instruments do not have broad band capabilities making other nuclei such as phosphorus inaccessible. Phosphorus NMR has been quite valuable in biological research. The use of tritium NMR is limited but increasing, and is valuable in determining position and distribution of label, radiochemical purity, and specific activity of labeled compounds that are often used in nutritional studies, metabolism studies, enzyme-substrate interactions, and radioimmunoassays. Because of radiation hazards, one facility should exist somewhere in ARS and should be accessible to all ARS scientists.

#### NMR Imager Spectrometers

Table 3 lists the costs of Magnetic Resonance Imager Spectrometers. One vendor indicated that larger imaging spectrometers require a specially fabricated facility in which to operate the spectrometers. Cost for a 4.2T imaging spectrometer was estimated at \$1,000,000. A facility to house the imager was estimated at \$1,000,000, while a facility to house an imager with a 1000 mm bore (for humans) was estimated at \$2,000,000. The cost of the 100 mm bore spectrometer itself also was estimated at \$2,000,000.





Table 1. NMR Spectrometers (~200 MHz) and Their Approximate Cost by Vendor.

<u>GENERAL ELECTRIC</u>		
QE-300	300 MHz (7.05T); 44 mm Bore 5 & 10 mm $^{13}\text{C}/^1\text{H}$ $^{31}\text{P}$ - $^{15}\text{N}$ Probe & Console	\$ 200,000 250,000
GN-300NB	300 MHz (7.05T); 54 mm Bore 5 & 10 mm $^{31}\text{P}$ - $^{15}\text{N}$ Probe	\$ 290,000
GN-300	300 MHz (7.05T); 89 mm Bore 5, 10 & 20 mm $^{73}\text{Ge}$ to $^1\text{H}$	\$ 350,000
GN-500	500 MHz (11.75T); 51 mm Bore 5 & 10 mm, 2 probes	\$ 615,000
<u>BRUKER</u>		
AM-250	250 MHz (5.87T); 54 mm Bore 5, 10 & 15 mm Probe; $^{109}\text{Ag}$ to $^{31}\text{P}$	\$ 225,000
AM-300	300 MHz (7.05T); 54 mm Bore 5, 10 & 15 mm Probe; $^{109}\text{Ag}$ to $^{31}\text{P}$	\$ 264,000
AM-300WB*	300 MHz (7.05T); 89 mm Bore 5, 10, 15, 20, & 25 mm Probe; $^{109}\text{Ag}$ to $^{31}\text{P}$	\$ 295,000
AM-400	400 MHz (9.4T); 52 mm Bore 5, 10 & 15 mm Probe; $^{109}\text{Ag}$ to $^{31}\text{P}$	\$ 410,000
AM-400WB*	400 MHz (9.4T); 89 mm Bore 5, 10, 15, 20, & 25 mm Probe; $^{109}\text{Ag}$ to $^{31}\text{P}$	\$ 450,000
AM-500	500 MHz (11.75T); 52 mm Bore 5, 10 & 15 mm Probe; $^{109}\text{Ag}$ to $^{31}\text{P}$	\$ 600,000
[*WB Magnets capable of <u>in vivo</u> NMR on rats]		
MSL-200†	200 MHz (4.7T); 89 mm Bore	\$ 290,000
MSL-300†	300 MHz (7.05T); 89 mm Bore	\$ 330,000
MSL-400†	400 MHz (9.4T); 89 mm Bore	\$ 461,000

[†Capable of solid state NMR, high resolution liquids, NMR imaging, and in vivo spectrometry]



JEOL

GX-270/54	270 MHz (6.34T); 54 mm Bore 5 & 10 mm Probe; $^1\text{H}/^{13}\text{C}$	\$ 205,000
GX-270/89	270 MHz (6.34T); 89 mm Bore 5 & 10 mm Probe; $^1\text{H}/^{13}\text{C}$	\$ 225,000
GX-400/54	400 MHz (9.4T); 54 mm Bore 5 & 10 mm Probe; $^1\text{H}/^{13}\text{C}$	\$ 300,000
GX-400/89	400 MHz (9.4T); 89 mm Bore 5 & 10 mm Probe; $^1\text{H}/^{13}\text{C}$	\$ 360,000

IBM

NR/200	200 MHz (4.7T); 50 mm Bore 5 & 10 mm Probe; $^1\text{H}/^{13}\text{C}$	\$ 200,000
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VARIAN

VXR-200	200 MHz (4.7T); 51 mm Bore 5, 10 & 16 mm Probe; $^1\text{H}/^{13}\text{C}$	\$ 130,000
VXR-200\$	200 MHz (4.7T); 51 mm Bore 5, 10 & 16 mm Probe; Multinuclear	\$ 225,000
VXR-300\$	300 MHz (7.05T); 51 mm Bore 5, 10 & 16 mm Probe; Multinuclear	\$ 325,000
VXR-400\$	400 MHz (9.4T); 51 mm Bore 5, 10 & 16 mm Probe; Multinuclear	\$ 425,000
VXR-500	500 MHz (11.75T); 51 mm Bore 5, 10 & 16 mm Probe; Multinuclear	\$ 625,000

[\$Solids (magic angle spinning) + \$40,000; Wide Bore (89 mm) + \$50,000  
for 200 MHz to + \$80,000 for 400 MHz]

MAGNACHEM

A-200	200 MHz (4.7T); 52 mm Bore 5 & 10 mm Probe; $^{31}\text{P}$ to $^{29}\text{Si}$	\$ 140,000
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Table 2. Approximate Cost of NMR Spectrometers by Magnet Size with Standard Accessories.\*

<u>Magnet</u>	<u>Cost</u>
200 MHz	\$150,000-\$300,000
300 MHz	\$200,000-\$380,000
400 MHz	\$360,000-\$500,000
500 MHz	\$600,000-\$625,000

\*Prices vary depending on capabilities (e.g. Solid probe capable of magic angle spinning, wide bore 89 mm magnets etc.).

Table 3. Magnet Resonance Imager Spectrometer Cost.

<u>System Name</u>	<u>Cost in \$</u>
<u>GENERAL ELECTRIC</u>	
CSI 2 (2T); 310 mm Bore	700,000
CSI 4.7 (4.7T); 330 mm Bore	1,000,000
<u>BRUKER</u>	
Biospec 310/1.9 (1.9T); 310 mm Bore	490,000
Biospec 400/2.3 (2.3T); 400 mm Bore	630,000
Biospec 300/4.7 (4.7T); 300 mm Bore	800,000
Biospec 400/4.2 (4.2T); 400 mm Bore	965,000



## Efficient and Effective Use of NMR Instruments

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It seems to me that any consideration of the efficient and effective use of NMR spectrometers should focus on the approximately 16 hours of each working day when the instrument is unattended. The extent to which the hardware and software provide a convenient means for running multiple samples under a variety of experimental conditions determines to a large degree the overall efficiency of the NMR laboratory.

The most important hardware component for unattended operation is a reliable and cost-effective sample changer. Every NMR manufacturer presently offers such a unit, but they are far from cheap. Several cost in the vicinity of 30 K\$. However, I submit that over the useful lifetime of supercon-NMR system they are cost effective even at their present cost. Systems have also been described utilizing a chemical robotic system which can be assembled at somewhat less initial cost but with the added cost of the time required to assemble the components and to program either the instrument computer or an auxiliary computer to reliably perform this function. Unless a computer applications group is available, this would not appear to be a cost effective alternative.

All current manufacturers of computer-controlled spectrometers provide some type of software for the stacking of multiple NMR experiments. They also provide a means for the automatic shimming of the magnetic field, a mandatory requirement when changing samples. I think it is very important for each prospective supervisor of a computer-controlled spectrometer to carefully evaluate the performance of this software in view of the way the instrument is to be utilized. If open-shop operation of the spectrometer is anticipated, then much more attention must be directed towards its ease of use. In general, I believe versatility should be sacrificed in order to insure reliable and convenient operation. The most sophisticated control program is worthless if the user cannot be 100 percent confident of its performance!

Besides the 16 night-time hours available during a regular working day, there are the 64 unattended hours available during a weekend period. The same sample handling and program-stacking capabilities can be employed to utilize this more extended unattended period. The reliability of modern solid-state instrumentation makes practical the utilization of such lengthy periods. Power failures represent the most likely cause of experiment interruption. Where these occur frequently during certain seasons, uninterruptable power sources represent a practical solution in view of the modest power demands of supercon spectrometer systems.

In order to evaluate the data accumulated during unattended periods while continuing to run samples on the system during regular work periods, serious consideration should be given to the provision of at least a second workstation. In this way, one operator can be setting up or running a short-term experiment





while another is evaluating or plotting data at a second station. Some recent NMR computer systems have been configured for two stations. With these, the cost of the second station is only that of a color or monochrome terminal and a plotter, which can be obtained for well under 10 K\$. Other systems require a separate CPU as well, which adds appreciably to the total cost. Further efficiencies can be achieved if the control program provides a telecommunications capability which permits a scientist to interact with an NMR experiment via a portable computer from home during an overnight or weekend run. In general, I feel we will see a marked drop in overall cost of satellite work stations in the next 1-2 years.

In summary, to maximize the utility of modern NMR instruments, considerable attention should be given to the facilities provided for unattended instrument operation and for the expeditious evaluation of the voluminous data produced during these periods. Three factors require special attention:

1. Automated sample changing.
2. Easy-to-use experiment-stacking programs.
3. One or more additional NMR work stations.
4. Overnight and weekend telecommunications link.



## Applications of NMR Imaging Spectroscopy in Agricultural Research:

### Animal Studies

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Advances in NMR spectroscopy and imaging techniques in recent years have resulted in the ability to probe the intact organism in a manner which was previously attainable only by invasive procedures or by the use of ionizing radiation. This technology is now being utilized in the field of human medicine where it is proving to be a valuable diagnostic procedure. The FDA currently restricts the medical application of NMR imaging (MRI) to a power of less than 2.0 T. Research instruments are now available which can operate at 4.7 T, thus greatly expanding their research capability. The potential of application of this technology for research in animal agriculture appears to be great and probably includes nearly every discipline within the field of animal science.

The following are just some of the potential uses of MRI in this area. Tissue and whole body composition could be studied in a non-invasive and non-destructive manner. NMR generated relaxation times can be used to measure water, lipid (Fullerton, et al., 1982 & 1985) and possibly collagen (Edzes & Samulski, 1978 and Fung & McGaughy, 1980) in vivo and in vitro. This would be particularly valuable for evaluating animals in concert with genetic selection and gene insertion experiments where traditional methods have been impractical or inaccurate.

Specific organ imaging may be useful in a number of studies. Information such as changes in blood flow or biochemical events in the hypothalamus may be useful to study seasonality of reproduction in sheep. Paramagnetic or isotopic labeling may be used to study nutrient or metabolite uptake in various organs. Organ abnormalities such as tumors, hemorrhages, edema or gross structure may be observed along with possible chemical information. Embryonic development and possibly fertilization can be observed (Merta, et al., 1985).

Real time measurements of a number of metabolic events could prove valuable for the study of both normal and abnormal biology in animals. NMR spectra of  $^{31}\text{P}$  can be used to show shifts in ATP, ADP, phosphocreatine and inorganic phosphorus (Fullerton & Cameron, 1985). Such changes may be related to enzyme deficiencies, anoxia or ischemia (Frahm, et al., 1985). Certain mineral ions in particular may lend themselves to NMR studies. For example, the absorption, transport and storage of various forms of iron could be visualized.

Also, within ARS a number of studies in human nutrition would benefit from these potential applications of MRI.

In summary, MRI appears to have significant potential for advancing the application of biotechnology in agricultural research.



## Applications of NMR Imaging Spectroscopy in Agricultural Research:

## Insect Studies

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Noninvasive studies of developing plant and animals have philosophical appeal and scientific merit. Studying a system noninvasively offers an opportunity to carry out research on living organisms in a nondestructive way. Developmental geneticists need to understand the sequential and compartmental processes in early embryonic development. Cryopreservationists need to identify chemical and structural changes that are critical to maintaining the integrity of the organism during freezing and thawing. Physiologists need to track relevant nuclei through plant and animal vascular systems. These and many other areas of in vivo research require the nondestructive methods available using nuclear magnetic resonance (NMR) technology. Proton NMR spectroscopy designed to combine imaging and selected volume spectral analysis offers great promise for research on developmental dynamics. I have used this NMR method (Image Selected In Vivo Spectroscopy, ISIS) to follow the course of development of the locust, Schistocerca gregaria (Forsk.) from a few hours post-fertilization to the formation of the first nymphal stage through subsequent hatching. This technique demonstrates that the dynamics of a developmental system can be visualized and chemically analyzed noninvasively. Embryonic movements, the formation of membranes, compartments, anatomical structures, and the dynamics of water and lipid in selected submicroliter volumes can be evaluated in a manner without precedent.

Generally, insect embryos develop in an isolecithal ooplasm, the yolk appears uniformly distributed within the egg's chorion. The first embryonic divisions take place in the yolk matrix. After several preblastoderm divisions, the products of fertilization form the presumptive embryonic germ band, and serosal and vitellogenic cells. In the locust, the germ band forms as a 300  $\mu\text{m}$  disc on the yolk periphery near the posterior dorsal margin. The remaining preblastoderm products form a membrane that envelops the embryo and yolk or lytic cells that digest the yolk. These cytological details and the subsequent features of the locust embryology were clearly established by light microscopy techniques. Now, proton NMR technology can form images of the developing embryo and analyze selected submicroliter volumes within the embryo and its yolk supply. Thereby, a new perspective of embryological development is gained. The microscopy and NMR spectroscopy images cannot be equated because of their different physical origins. However, given a thorough understanding of the positional distribution of cells and tissues in the developing embryo from microscopy, then in vivo NMR spectroscopy opens a new avenue for studying the dynamic process of embryogenesis.





## Applications of NMR Imaging Spectroscopy in Agricultural Research:

### Plant Studies

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The direct observation of plant roots will contribute to a better understanding of root growth and function. Nuclear magnetic resonance (NMR) imaging is the only noninvasive approach that allows a spatial image of the root system to be repeatedly formed in situ. Flow in plants may also be observed. Thus, growth dynamics and physiological processes involving flow may be studied. NMR images of Vicia faba L. seedlings show that NMR imaging promises to be an effective tool in solving plant root system problems. A requirement for NMR imaging research in plant research is clear.

Water (hydrogen nuclei) can be imaged by NMR, and provides an excellent means of studying root-soil-water relationships. Any stimulation or stress that affects root growth or flow processes may be a suitable candidate for investigation.

This approach allows the roots within a volume of soil to be visualized without disturbance. This, in turn, permits root growth to be monitored. The rooting media which often contains a much lower concentration of water than the roots can essentially be made transparent to the observer. Images can be made repeatedly over the life of the plant, resulting in a dynamic picture of response. Since it is non-specific, any factor influencing roots could be studied, factors such as soil aeration, soil temperature, irrigation, nutrition, and compaction. Secondary effects from leaf processes could also be researched, such as growth enhancement by elevated carbon dioxide, injury by herbicides or phytotoxic pollutants, and effects of disease organisms. Metabolic processes that involve flow, especially water flow, certainly can be studied.

In the case of flow studies within plants, contrast agents acting as tracers will greatly add to the utility of such measures. Paramagnetic ions (e.g.,  $\text{Cu}^{++}$ ,  $\text{Mn}^{++}$ ,  $\text{Gd}^{+++}$ ) act as contrast agents by decreasing the relaxation times of hydrogen nuclei, thus enhancing the NMR signal. Such materials, compatible with plant function, will need to be identified.

Another consideration in applying NMR imaging to root system problems is the soil matrix itself. Since the presence of magnetic materials can cause distortion, the distribution and quantity of magnetic soil components will be important. Soil water content will also be a factor since hydrogen nuclei are currently the best material to image. Images of roots in fully saturated soil would be difficult to resolve with NMR machines that are now available. However, images of  $^{19}\text{F}$ ,  $^{31}\text{P}$ , and  $^{23}\text{Na}$  can be made if present in sufficient concentrations.

The NMR image provides a spatial record of the water concentration throughout the soil/root system. The procedure is entirely non-destructive and has no



known effect on plants. Therefore, it can be repeated any number of times thus allowing growth and development to be followed. Sequential observation of roots in situ within the soil matrix along with direct measurements of the distribution of water have not been available until now. Clearly then, NMR imaging can be an effective tool in solving plant problems.



## Criteria for Giving NMR Collaborators Recognition

### Part I

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Athens, Georgia

Before having a discussion of the criteria for collaboration, we must define it and describe the various types that are possible for ARS. For the purposes of this discussion, collaboration is two or more parties conducting research that is of mutual interest, compatible with the goals of the organizations involved, the results of which are mutually beneficial to all involved.

The following is a list of the various types of collaboration that are envisioned as possible:

#### A. Within the Agency

1. You are an ARS scientist doing NMR spectroscopy and are collaborating with another ARS scientist that is providing the sample.
2. You are an ARS scientist providing the sample to another scientist in ARS who is doing NMR spectroscopy.

#### B. Outside the Agency

1. You are an ARS scientist doing NMR spectroscopy and collaborating with another scientist at an academic institution, industry, or other facility, e.g., NSF, who is providing you the sample.
2. You are an ARS scientist and are collaborating with an NMR spectroscopist who is associated with an academic institution, industry, or other facility.

In any collaborative research, serious consideration must be given to the level of recognition that each collaborator should receive. This will depend on their level of expertise required and the extent of their contribution (in terms of planning, execution, data interpretation and writing of conclusions). Determination of the degree of recognition to be received is probably best worked out on a scientist-to-scientist level and should, in general, be agreed upon prior to initiating collaboration or as soon as possible after very preliminary investigations.

The following types of recognition should be considered:

1. Senior authorship of manuscript.
2. Co-authorship of manuscript.
3. Acknowledgment on manuscript.
4. Credit on a patent.



Authorship of publications should follow the general guidelines of USDA-SEA Directive 152.2 (Authorship of Research and Technical Reports and Publication) in any type of collaborative work involving ARS. Obviously, if the work entails primarily structural elucidation by sophisticated NMR techniques and only routine isolation or synthesis techniques, the primary credit (i.e., senior authorship) should go to the NMR spectroscopist. Likewise, if obtaining the sample required extremely difficult or unusual procedures for isolation or synthesis and the NMR results were only incidental or nonroutine in nature, then the NMR spectroscopist deserves consideration for co-authorship or possibly only an acknowledgment on a manuscript. These are rather clearly defined situations and should really cause no problems with the collaborators.

The real problems come when both isolation or synthesis and structural proof are at the same level of difficulty. When this occurs, it becomes difficult to determine who should receive the primary credit. Often this can be resolved by multiple publications (one covering isolation or synthesis and one covering the structural proof). However, if the same techniques are used repeatedly for a series of publications, then "flip-flopping" of authorship should be considered.

The situation with patents is a little more difficult to resolve. Here one might ask the question: "Is it the sample or the proof of its structure that is important to guard?" In reality it is neither, but the potential use of the materials is important. Thus, the primary credit should go to the person that realized the potential. Normally, this is the one who saw the need to study the sample in the first place. The discussion of patents, at first glance, may not be germane to the subject at hand, but does point up the need to restrict collaborative work on potentially patentable items to within the Agency as much as possible. The person who "cracks" the structure will have the first knowledge about it. This would probably be the NMR spectroscopist in this case. Thus, this type of recognition needs to be restricted as much as possible to collaboration within the Agency, or at least cooperation within the U. S. Government.

Within the Agency. In conducting collaborative work within the Agency, it is important to recognize that the NMR spectroscopist should not only be given consideration for senior authorship of a publication when it involves a new instrumental technique, but also in situations that involve established techniques that require considerable knowledge to plan, execute, and interpret the results. The employment of many modern spectroscopic techniques and their subsequent utilization for structural elucidation should not always be considered simply a service that is ancillary to obtaining the sample. Both may often be true research and should be recognized as such. The recognition of this within ARS will go a long way to foster true collaboration and cooperation, thus allowing each scientist to do what they are best at doing. The primary function of the individual doing the NMR spectroscopy must also be considered in giving recognition within the Agency. If the spectroscopist is a Category I scientist, he cannot afford to do much service-type work but must seek situations that involve true collaboration and will afford him higher recognition. Too many co-authorships will not provide enough recognition when it comes time for overall evaluation of his work. Consideration must also be given to the mission that the spectroscopist has been given as a scientist according to the Current Research Information System (CRIS) and within a





Management Unit, if there is to be an extensive amount of time devoted to collaboration. If the situation is not handled properly, no amount of recognition will protect the spectroscopist from the results of too much collaboration outside of the projects involved with his primary assignment.

Outside the Agency. Collaboration outside the Agency must be treated with extreme care and should involve more formal consideration to the question of recognition prior to involvement in the work. If the situation involves funds, it falls outside of our definition of collaboration and will normally be covered by a cooperative agreement or contract. In those cases the document should fix the recognition to be received by each contributor.

An example of collaboration outside the Agency might be that done between an ARS scientist and a regional NMR facility (supported by NSF). This would require a proposal to be presented for consideration of the project to the NSF facility and that proposal would include the provision that the results be published in the open literature with the specified authors. Proprietary work (as may be required for patentable work) could not be handled this way and would have to be handled by the cooperative agreement method, if it was done with the same facility. That set-up would not provide for interpretation of the results and would more appropriately be labeled a service for which the facility and NSF would be only acknowledged, but also paid some fee.

Another example might be collaboration between an ARS scientist doing NMR spectroscopy with a synthetic organic chemist at a university to obtain information on a compound of mutual interest. Here, no exchange of money is deemed necessary, thus a formal agreement may not be necessary. In this situation, if the ARS scientist obtains and interprets the NMR data, the scientist should be afforded co-authorship, as a minimum, and senior authorship, if the scientist prepares the majority of the manuscript. If the situation is reversed, the ARS scientist should be prepared to accept the comparable recognition.

Collaboration between ARS and industry usually can only be very minor in nature without involving a formal cooperative agreement. The extent of this involvement may include running one or two spectra to check out the feasibility of pursuing research in a more formal arrangement. The recognition for this would be acknowledgment in an informal report.



## Criteria for Giving NMR Collaborators Recognition

## Part II

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In the absence of a central ARS-supported NMR facility, collaboration has been carried out by informal arrangements. NSF and NIH supported NMR regional facilities encourage collaboration between users and staff personnel. Regional facilities have not solved the problem of the remote user who because of time and/or financial constraints is unable to be present when samples are analyzed.

Anyone who actively participates in determining experimental conditions, data acquisition, data processing, and sample preparation deserves recognition. The form of recognition may be an acknowledgment if the collaboration is limited to the most routine data acquisition. If the advice and assistance of NMR personnel goes beyond the routine data gathering, then coauthorship in the resulting publication should be mandated.

Criteria for determining whether recognition is limited to acknowledgment or extended to coauthorship includes the following:

1. Information
2. Experiments
3. Planning
4. Complexity
5. Time
6. Writeup.

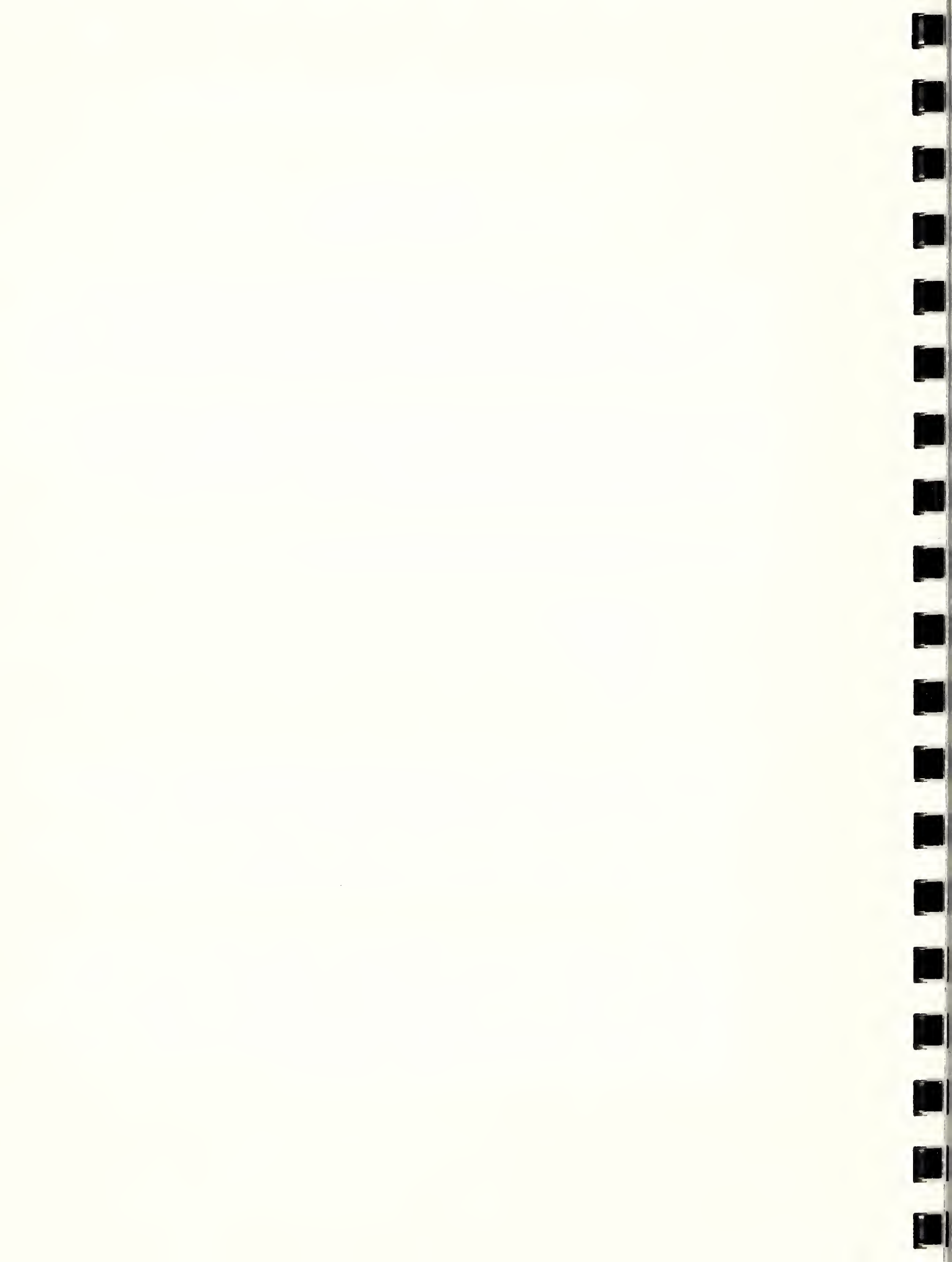
1. Information

A clear, concise statement of the required information is a necessary first step. An example of a routine collaboration; Obtain a proton and carbon 13 spectrum for each sample to compare with published data.

A more extensive collaboration might read; Determine the structure of the unknown natural product using as many NMR experiments as necessary.

2. Experiments

Even complex experiments are becoming more routine with new hardware and software. Extensive collaboration may be necessary to limit the number of experiments to those sufficient to solve the problem at hand. Routine experiments consist of an integrated proton spectrum, a broadband decoupled carbon 13 spectrum, and an experiment to determine the carbon multiplicities. Experiments which are/or will soon be routine include homonuclear (COSY) and heteronuclear correlation.



### 3. Planning

Planning an experiment can be limited to routine use of a standard set of parameters or parameters may have to be adjusted to optimize the information content. Solvents can be varied or mixed to give a clearer spectrum, for example.

### 4. Complexity

If the problem requires input from the NMR investigator as when, for example, quantitative information is needed for components in a mixture or stereochemistry needs to be defined by NOE experiments, then collaboration is beyond routine.

### 5. Time

Time includes not only machine time, which has to be carefully coordinated, but planning, preparation, and processing time must be considered. With experience, time may be estimated for a particular investigation. Clearly, time is a more important criteria for a fee-for-service arrangement when compared to collaboration.

### 6. Writeup

The writeup may consist of filling in a form for transmittal with raw data or it could extend to written evaluation and interpretation of data to be included in publications. Any writeup that is included in a paper calls for coauthor recognition.

### Summary

NMR equipment has become very sophisticated, complex, and expensive. A mechanism for optimizing the acquisition and use of new and existing NMR equipment is a necessary outgrowth of the heightened interest in NMR which extends beyond chemistry and into biotechnology. Collaborative research will have to play an important role if NMR is to be available to researchers physically and financially removed from hands-on use. To encourage collaborative research it may be necessary to establish a central ARS NMR facility with state-of-the-art equipment including funds for upgrading. Personnel staffing such a facility would be encouraged and rewarded for interacting with agency scientists to ensure the widest distribution of NMR capabilities.





# Selection of NMR Spectrometry and Imaging on a Merit of Proposal Basis

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## General Guidelines:

What kind of NMR studies does the work warrant?

- A. Nuclide(s) of interest
- B. Class of NMR experiment

e.g.  $^{13}\text{C}$  CPMAS  
 $^{15}\text{N}$  liquids  
 $^1\text{H}$  imaging

If high field spectra (500 MHz  $^1\text{H}$  spectra) are desired, indicate why low field (e.g., 100 MHz) spectra would not be adequate?

- A. Require that low-field spectra be included in the proposal to justify higher-field instrument usage.

What is the chemical or physical question or hypothesis which is being addressed?

- A. Structure
- B. Dynamics
- C. Conformation

What is the NMR question to be answered, and does it actually pertain to the chemical or physical hypothesis addressed above?

- A. What particular splitting or line position is of interest?
- B. Which relaxation parameter is of major importance?
- C. Is thermodynamic or variable temperature (VT) work necessary?

## Proposal Evaluation Criteria:

A specific format for the evaluation of NMR spectroscopy and imaging projects does not appear to be desirable, nor can such evaluations be categorically streamlined into a common pattern suitable for every case.

The real value of proposals lies in their elements of individuality and originality.

However, the following aspects of proposals might be considered in order to provide some degree of common coverage.

1. Research performance competence



- A. Capability of the investigator(s)
  - B. Recent research performance of the investigator(s)
  - C. Technical soundness of the proposed research
  - D. Adequacy of the institutional resources
2. Scientific merit and originality of the proposal
- A. Likelihood that the research will lead to new discoveries or fundamental scientific advances
  - B. Potential impact of basic research on future technology
3. Utility or relevance of proposal
- A. Solution of critical problems
  - B. Contribution(s) to progress in scientific areas which are extrinsic or in addition to the research itself, the results of which may lead to future applications.

Criterion 1 - Research performance competence - essential to the evaluation of the quality of any research proposal

Criteria 2 and 3 - The relative weight assigned to these categories depends directly on the nature of the proposed research

- A. Criterion 2 - Intrinsic merit, is emphasized when evaluating basic, fundamental research proposals.
- B. Criterion 3 - Utility or relevance is emphasized in evaluating applied research proposals.

#### Conflict of Interest(s)

An affiliation or connection with the institution or person submitting the proposal might be construed as a conflict of interest.

An independent evaluator of a proposal should not have any conflicting bias, affiliation, or interest in the proposal itself.

#### Facility Utilization

1. REMOTE SERVICE - User submits samples and does not participate in any manner in the NMR experiments.
2. PARTICIPATORY SERVICE - User is present during the experiments, participates, and works with staff who are actually operating the spectrometer(s).
3. INDEPENDENT USE - User is trained and proficient in the operation of the spectrometer(s), and reserves time for the experiments.
4. COLLABORATION - User establishes a mutually beneficial, active collaboration with an NMR staff member compatible with the mission of the facility.



Access to a spectrometer or NMR facility might also depend upon the user participation mode as described above.

Furthermore, NMR proposals may or may not be consistent with NMR facility budgets, and thus be placed at a disadvantage when competing for limited spectrometer time.

Finally, in the selection of NMR spectroscopy and imaging projects on a merit of proposal basis, certain costs would have to be considered.

- A. Overhead and Maintenance
- B. Spectrometer Time and Reimbursement
- C. Technical Staff Support
- D. Equipment Modification
- E. Solvents, Tubes, Discs, Expensive Supplies, and Handling



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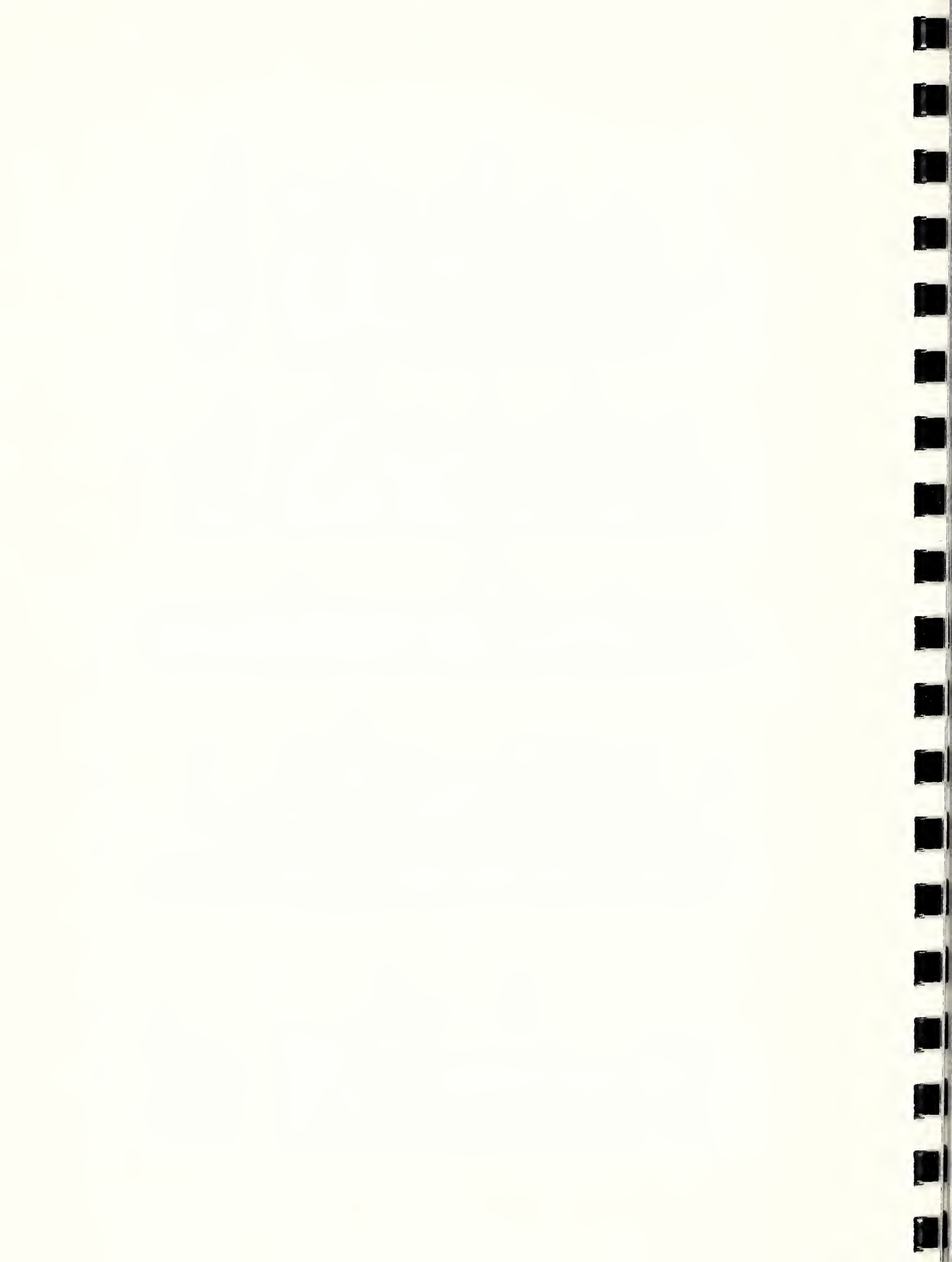
Weisleder, David (360-4304)  
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 Analytical Chemistry Support Unit  
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## Appendix A

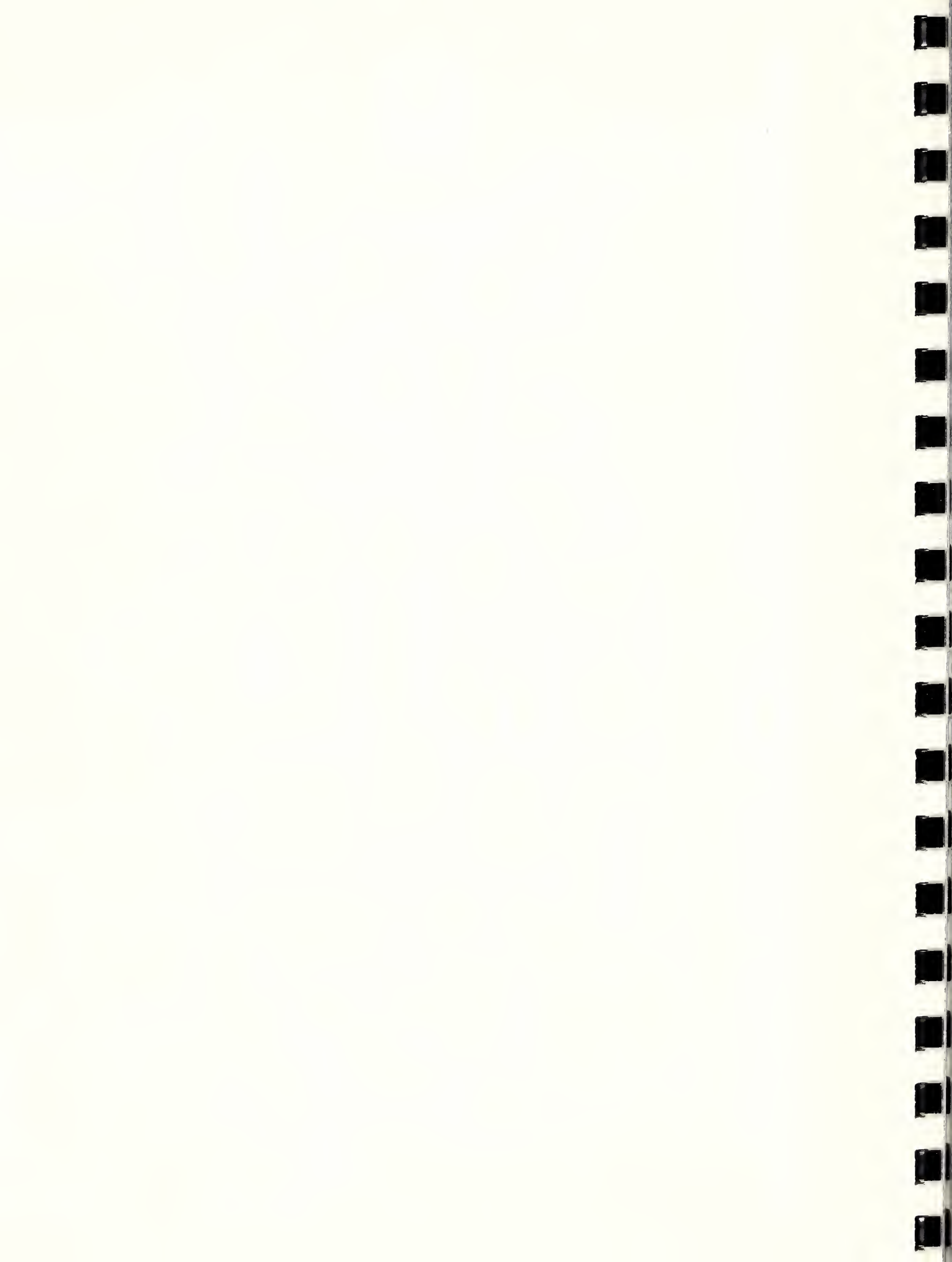
<u>Instrument</u>	<u>Contact</u>	<u>Phone #</u>	<u>Location</u>	<u>Discipline</u>
Bruker WH-90	Weisleder, David	360-4304	Peoria, IL	Anal. Chem. Support Unit
Bruker WM-300 WB	Weisleder, David	360-4304	Peoria, IL	Anal. Chem. Support Unit
Bruker 90MHz	Mount, Gary	947-7900	Kerrville, TX	Tick Res.
IBM mini spec	Whiting, Dick	489-6437	Philadelphia, PA	Food Sci. Lab.
IBM mini spec	Himmelsbach, David	250-3196	Athens, GA	Field, Crops Res.
JEOL FX-60	Horowitz, R. (Bob)	213-681-7294	Pasadena, CA	Fruit & Veg. Chem. Res.
JEOL FX90Q	Ellzey, S. E.	682-7561	New Orleans, LA	Comp. & Prop. Res.
JEOL FX60Q	Thompson, Malcolm J.	344-2389	Beltsville, MD	Insect Physiol.
JEOL FX90Q	Stipanovic, Robert D.	527-1233	College Sta., TX	Cotton Pathol. Res.
JEOL PFT 100	Lundin, Robert. E.	449-3444	Berkeley, CA	Chem. & Struct. Res.
JEOL PS/PFT 100MHz*	Himmelsbach, David	250-3196	Athens, GA	Field, Crops Res.
JEOL GX270 (solids)	Horowitz, R. (Bob)	213-681-7294	Pasadena, CA	Fruit & Veg. Chem. Res.
JEOL 400MHz	Pfeffer, Philip	489-6635/6469	Philadelphia, PA	Plant & Soil Biophysics
JEOL 60MHz (solids <sup>13</sup> C)	Pfeffer, Philip	489-6635/6469	Philadelphia, PA	Plant & Soil Biophysics
JEOL FX90Q	Feil, Vernon J.	783-5423	Fargo, ND	Met. Rad. Res. Lab.
Newport Oil Anal.	Seiler, Gerald J.	735-6721	Bushland, TX	Sunflower Res.
Newport Wide-Line	Kohel, Russell J.	527-1311	College Sta., TX	Cotton Pathol. Lab.
Nicolet 200MHz, 89mm	Lundin, Robert. E.	449-3444	Berkeley, CA	Chem. & Struct. Res.
Nicolet 300, 54mm	Tumlinson, James H.	947-7730	Gainesville, FL	Insect Chem. Res.
GE QE300, 44mm	Warthen, J. David, Jr.	344-1981	Beltsville, MD	Insect Chem. Ecol. Lab.
Varian CFT-20	Boudreaux, Gordon	682-7048	New Orleans, LA	Comp. & Prop. Res.
Varian EM-390	Lundin, Robert. E.	449-3444	Berkeley, CA	Chem. & Struct. Res.
Varian Em-360L	Keeler, Richard F.	801-752-2941	Logan, UT	Poisonous Plant Res.
Varian EM-360L, 60MHz	L. Wartelle (Pepperman, A.)	682-7564	New Orleans, LA	Crop Protect. Chem.
Varian T-20	Hedin, Paul	682-7564		
Varian T-20	Thompson, Alonzo C.	497-1145	Miss State, MS	Cotton Host Plant Resist.
Varian T-60A	Patton, Steven H.	497-1144	Miss State, MS	Cotton Host Plant Resist.
Varian VXR-200	Ellzey, S.	467-5337	Fresno, CA	Water Mngt. Res.
(solids <sup>16</sup> N-31p)	(Berni, R.)	682-7097	New Orleans, LA	Comp. & Prop. Res.
Varian XL100	Mills, Frank	682-7547		
		344-2531	Beltsville, MD	Anal. Chem. Lab.

\*ARS solids probe on Univ. Georgia FX270 also available.



# Agricultural Research Service - NMR Instrument Distribution







# Appendix C

<u>Area Contacts</u>	<u>*Instrumentation</u>	<u>Personnel</u>
<u>North Atlantic</u> Pfeffer and Gerasimowicz	200 MHz MSL solid instrument with imaging option Remote processing and sample change capability for 400 MHz	One master level physicist
<u>Southern Plains</u> Stipanovic	Purchase widebore 300 MHz instrument	One master level chemist
<u>South Atlantic</u> Himmelsbach	Purchase 200 MHz solid with option for imaging	One master level chemist
<u>South Atlantic</u> Cutler and Cole	Access to NMR instrumentation	One Ph.D. spectroscopist
<u>Beltsville - Mitchell</u> <u>Northwest - Stellflug</u> <u>South Atlantic - Rogers</u>	Establish cooperation outside of ARS to acquire access to one meter bore imaging system	Collaborators
<u>Northern States</u> Feil and Gassner	Purchase one 300 to 400 MHz instrument Acquire access to small imaging systems	One master level physicist
<u>Pacific Basin</u> Lundin	Purchase one 400 MHz instrument	Collaborators
<u>Midwest</u> Weisleder	Purchase highest field instrument available with sample changer and remote processing	Collaborators
<u>Mid South</u> Berni		One master level chemist

\* Delivery time is about 12-18 months for 200-400 MHz and about 2 years for 500 MHz instruments.  
Support from the FY 88 budget would mean first deliveries around the year 1990.





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